

### Remarks

Claims 22-34 are pending in the subject application. By this Supplemental Preliminary Amendment, claims 22-34 have been canceled and new claims 35-56 have been added, which read on the elected invention. Accordingly, claims 35-56 are currently before the Examiner. Support for the new claims can be found, for example, in the claims as filed in the PCT applications, the claims presented via the first preliminary amendment and page 8 of the as filed specification. Favorable consideration of the pending claims is respectfully requested.

A new set of claims has been submitted in response to the Restriction Requirement of March 29, 2007. The new set of claims is drawn to altered polypeptides of human mature MCP proteins (or fragments thereof) having an antagonistic activity to MCP proteins. The altered polypeptides contain mutations of at least following amino acids:

- a. positions 18 and 19;
- b. positions 18, 19, and 58;
- c. positions 18, 19, and 66;
- d. positions 18, 19, 58, and 66; and
- e. positions 18, 19, and one or more of the following: 24, 44, 49, 75.

Thus, the antagonists of MCP proteins provided in the new set of claims are all based on a polypeptide containing mutations of at least amino acids at positions 18 and 19, as numbered on the sequence of mature human MCP-1. Therefore, the claimed sequences are related in structure and relate to a single general inventive concept. Applicants also respectfully submit that the claimed invention complies with the definition of "special technical feature" as it defines a contribution over the prior art (*i.e.* Hemmerich *et al.*).

Hemmerich *et al.* discloses the identification of regions of MCP-1 that contact its receptor, CCR2. For that purpose, all surface-exposed residues were substituted with alanine to analyze the difference in receptor binding (page 13017, left-hand column). Hemmerich *et al.* teaches that the majority of point mutations had no effect on the receptor binding. However, two clusters of primarily basic residues (R24, K35, K38, K49 and Y13) reduced the level of receptor binding by 15- to 100-fold. The paragraph bridging pages 13016 and 13017 shows that mutations in positions 18 or 19

alone are not sufficient to yield antagonists (see also page 13022, right-hand column). Mutants with several mutations are also disclosed (Figure 3, page 13017) but not one of the mutated polypeptides includes the double mutation of residues 18 and 19. Therefore, the common concept linking the new claims (*i.e.* at least the double mutation of residues 18 and 19) is novel over Hemmerich *et al.* Accordingly, the double mutation in the claimed MCP polypeptide is a special technical feature according to PCT Rule 13.2 and links all presently appearing claims by a single inventive concept under PCT Rule 13.1. Accordingly reconsideration and withdrawal of the restriction requirement set forth in the paper mailed March 29, 2007 is respectfully requested.

Applicants believe that the pending claims are in condition for allowance and such action is respectfully requested.

Applicants invite the Examiner to call the undersigned if clarification is needed or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Respectfully submitted,



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